REMARKS

The claims, upon entry of the above amendment, are 1, 2, 5, 7 and 9 to 12.

The above amendment is responsive to points set forth in the Official Action.

In this regard, claim 1 has been amended to recite the porous, spherical calcium carbonate carrier as "having a relative surface area of 1.5 m^2/g or greater (BET method)". Support is evident from the disclosure at page 6, lines 5 and 6 of the present specification.

Further, it is now recited in claim 1 that the claim formulation is one wherein the insulin is adsorbed or carried as a monolayer or multilayer. Support is evident from the disclosure at page 6, lines 11 and 12 of the specification.

Lastly, the feature of claim 4 has been incorporated in claim 1.

The significance of the above amendment will be apparent from the remarks below.

Claims 1-12 were rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagawa (EPO 0 681 833 A2) in view of Staniforth et al. (USPN 5,948,438).

This rejection is respectfully traversed.

A brief discussion of the present invention will be of assistance in appreciating Applicant's reasons for traversal of the rejection.

The present claims recite that the "porous-spherical" calcium carbonate of the present invention has a feature as disclosed in the present application at page 6, lines 5 and 6 regarding the relative surface are and is clearly distinguishable from "standard light calcium carbonate available on the market, which is usually 0.1-0.3 m^2/g", as is stated in the description, page 6, lines 6-8.

Thus, on page 6, lines 4 to 8 of the present specification, it is disclosed that "the calcium carbonate used in connection with the present invention is characterized by having a relative surface area of 1.5 m^2/g or greater (BET method). This is significantly higher than that of standard light calcium carbonate available on the market, "which is usually 0.1-0.3 m^2/g."

It will be noted that the foregoing surface area was originally claimed in claim 8 and thus does not introduce a new issue.

Turning to the cited references, Yanagawa discloses calcium carbonate only as an example of "physiologically acceptable powdery or crystalline polyvalence metal compound carriers", and

makes no mention of the properties of the calcium carbonate. It would be clear therefore that the calcium carbonate which was mentioned in Yanagawa was such one as available and standard at the time when the invention of Yanagawa was made. Besides, the phrase "physiologically acceptable" suggests that the calcium carbonate of Yanagawa is the same as, or equivalent to "pharmacopeial product" which is mentioned in the description, page 8, line 12.

In Staniforth et al., on the other hand, it is disclosed in column 17, lines 56-63, for example that:

"...the inert pharmaceutical filler comprises...calcium carbonate..."

In column 19, lines 9-11, it is mentioned as follows:

"acidity reducing agents (e.g., buffering agents, such as...calcium carbonate..."

Thus, it would be clear from the above-quoted passages that the calcium carbonate to be used in Staniforth et al. was a standard one.

Replying to the comments on pages 4-6 of the Official Action:

In Yanagawa, page 2, lines 44-46, it is disclosed that:

"The present invention has the primary object to provide a nasally administrable composition to nasally administer such a physiologically active peptide or other physiologically active substances as unlikely to be administered orally..." (emphasis added)

Staniforth et al., on the other hand, mainly discloses an invention which relates to "oral solid dosage form" (ABSTRACT). Hence, anyone skilled in the art would have understood that Staniforth et al. and Yanagawa are directed to very different objectives. It is therefore unreasonable to combine these two references with each other, even for the sake of argument.

From page 3, line 10 to page 4, line 2, in particular page 3, lines 17-20, of the Official Action it is stated:

"Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use porous particles of calcium carbonate as a carrier because they can provide better performance and be more cost effective than various carriers."

"Porous" material which is used in Staniforth et al. is, however, "porous particles of microcrystalline cellulose" (see page 3, line 15), which are very different from calcium carbonate, i.e., inorganic compound.

At page 3, lines 13-15, the Official Action states as follows:

"Staniforth et al. teach pharmaceutical formulations having improved disintegration and/or absorptivity wherein calcium carbonate is used in combination with porous particles of microcrystalline cellulose..."

The above-quoted statement is untenable. The reasons are as follows. In Staniforth et al., column 19, lines 37-43, it is disclosed:

"In further embodiments of the invention,...provide improved disintegration properties (such as colloidal silicon dioxide) and a second augmenting agents for improving absorptivity (and consequently bioavailability) (for example, sodium lauryl sulfate)." (emphasis added)

Thus, what improves absorptivity is sodium lauryl sulfate (surfactant), which is very different from calcium carbonate.

Hence, no art-skilled person would have motivation for using porous particles of calcium carbonate in consideration of Staniforth et al., for the following reason:

"The expected result would be a highly effective pharmaceutical formulation having improved disintegration and/or absorptivity as similarly desired by the applicant." (page 3, line 1 from the bottom to page 4, line 2 of the Official Action)

Regarding the contentions of the Official Action at page 4, line 6 to page 5, line 7:

As stated above, neither Yanagawa nor Staniforth et al. mention or suggest the use of porous particles of calcium carbonate. Nor is there any passage in Staniforth et al. to suggest that the use of porous particles of calcium carbonate improves disintegration and/or absorptivity of pharmaceutical formulation. (see the above-quoted column 19, lines 37-43, of Staniforth et al.)

On the contentions at page 5, line 8 to page 6, line 4 of the Official Action:

As stated above, neither Yanagawa nor Staniforth et al. mention or suggest the porous particles of calcium carbonate which is used in the present invention.

Furthermore, it would have been impossible to foresee, from these references, the effects which would be produced by the use of such porous particles.

As is seen in Table 2 at page 9 of the present specification, for instance, $PSCaCO_3$ 20-32 μm has a C_{max} value (maximum concentration of medicine in blood) of 403.47 ± 43.60, i.e., about twice as high as 218.22 ± 28.93 which is C_{max} value of non-porous $CaCO_3$ 20-32 μm. Thus, $PSCaCO_3$ 20-32 μm has significantly high effects.

According to Fig. 4, on the other hand, among porous calcium carbonate, $PSCaCO_3$ 20-32 μm shows remarkably higher blood insulin concentration as compared with PS 18-115 μm, in particular with PS 20-38 μm.

Thus, porous particles of calcium carbonate which has an average particle size of 20-30 μm have effects which are unexpected even from PS 20-38 μm which contains only a little larger particles.

Such being the case, the present invention, in particular the present invention as defined by previous claim 4 now incorporated in claim 1, is unobvious from Yanagawa and Staniforth et al. alone or combined.

Regarding contentions at page 6, lines 5-17 of the Official Action:

To be sure, Staniforth et al. teach the idea of using calcium carbonate in combination with insulin. As stated above, however, Staniforth et al. neither disclose nor suggest the use of porous particles of calcium carbonate. Nor do Staniforth et al. suggest that calcium carbonate improves "disintegration and/or absorptivity" of pharmaceutical formulation.

For the foregoing reasons, it is apparent that the rejections on prior art are untenable and should be withdrawn.

No further issues remaining, allowance of this application is respectfully requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact undersigned at the telephone number below.

Respectfully submitted,

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